

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference  60001 PCT	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No.  PCT/US 03/40878	International filing date (day/month/year)  19/12/2003	(Earliest) Priority Date (day/month/year)  19/12/2003
Applicant  NEUROGEN CORPORATION		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 7 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

SUBSTITUTED BIARYL-4-CARBOXYLIC ACID ARYLAMIDE ANALOGUES AS CAPSAICIN RECEPTOR MODULATORS

5. With regard to the **abstract**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. \_\_\_\_\_

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

# INTERNATIONAL SEARCH REPORT

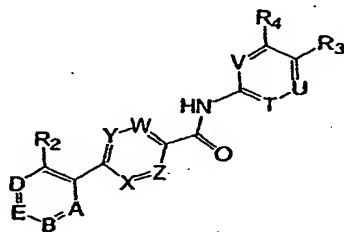
International application No.

PCT/US 03/40878

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

## ABSTRACT OF THE DISCLOSURE

Substituted biphenyl-4-carboxylic acid arylamide analogues of the formula:



capable of modulating receptor activity, are provided. Such ligands may be used to modulate receptor activity *in vivo* or *in vitro*, and are particularly useful in the treatment of pain and other conditions associated with receptor activation in humans, domesticated companion animals and livestock animals. Pharmaceutical compositions and methods for treating such disorders are provided, as are methods for using such ligands for receptor localization studies.

## INTERNATIONAL SEARCH REPORT

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## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D213/61 C07C235/64 C07D213/82 C07D213/26 C07D213/48  
 C07D405/12 C07D213/73 C07D211/34 C07D213/76 A61K31/44  
 A61P25/00 C07D417/12 C07D401/12 C07D405/04 C07D405/14

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D C07C A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 496 378 A (THOMAE GMBH DR K) 29 July 1992 (1992-07-29) example 10(13)claims 1,7-9	71,75
X	EP 0 480 258 A (BAYER AG) 15 April 1992 (1992-04-15) claim 1; examples 478,479,493,494	71,75
X	SIGMAN, MICHAEL E. ET AL: "Aroylnitrenes with singlet ground states: photochemistry of acetyl-substituted aroyl and aryloxycarbonyl azides" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY , 110(13), 4297-305 CODEN: JACSAT; ISSN: 0002-7863, 1988, XP002289185 page 4305 N-cyclohexyl-4-acetyl-4'-biphenyl- carboxylic acid amide	71
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☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \* & \* document member of the same patent family

Date of the actual completion of the international search

5 August 2004

Date of mailing of the international search report

16/08/2004

Name and mailing address of the ISA

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# INTERNATIONAL SEARCH REPORT

International Publication No

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KEIR W F ET AL: "Ethyl amidinoacetates in the synthesis of pyrazines" JOURNAL OF THE CHEMICAL SOCIETY, PERKIN TRANSACTIONS 1, CHEMICAL SOCIETY. LETCWORTH, GB, 1978, pages 1002-1006, XP002284500 ISSN: 0300-922X compound 3t	71
X	U. LUECKING ET AL.: "Self-folding cavitanads of nanoscale dimensions" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY., vol. 122, no. 37, 2000, pages 8880-8889, XP002289464 USAMERICAN CHEMICAL SOCIETY, WASHINGTON, DC. compound 12	71
X	PREVOT-HALTER, ISABELLE ET AL: "Assembling Organic Receptors around Transition Metal Templates: Functionalized Catechols and Dioxomolybdenum(VI) for the Recognition of Dicarboxylic Acids" JOURNAL OF ORGANIC CHEMISTRY ,VOL. 62, NO. 7, 1997, PAGES 2186-2192CODEN: JOCEAH; ISSN: 0022-3263, 1997, XP002289184 compounds 1 and 10	1
A	WO 03/068749 A (MITCHELL DARREN JASON ; RAMI HARSHAD KANTILAL (GB); GLAXO GROUP LTD (G) 21 August 2003 (2003-08-21) claims 1-9; examples	1-119
A	WO 02/08221 A (BAKTHAVATCHALAM RAJAGOPAL ; DESIMONE ROBERT W (US); NEUROGEN CORP (US)) 31 January 2002 (2002-01-31) the whole document	1-119
A	SZALLASI A ET AL: "VANILLOID (CAPSAICIN) RECEPTORS AND MECHANISMS" PHARMACOLOGICAL REVIEWS, WILLIAMS AND WILKINS INC., BALTIMORE, MD,, US, vol. 51, no. 2, 1999, pages 159-211, XP001105620 ISSN: 0031-6997 abstract	1, 17, 30, 45, 60, 65, 70, 71, 113-119

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## Continuation of Box I.1

Although claims 77-105 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

## Continuation of Box I.2

Claims Nos.: 71 (part.)

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of the claim(s) may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claim(s) is impossible. Consequently, the search has been restricted to: claims 1-70,72-119. The large number of relevant documents for claim 71 precludes a comprehensive search report.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 03/40878

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 77-105  
because they relate to subject matter not required to be searched by this Authority, namely:  
Although claims 77-105 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 71 (part.)  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 03/40878

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 0496378	A	29-07-1992	DE 4102024 A1	30-07-1992
			AT 128120 T	15-10-1995
			AU 648379 B2	21-04-1994
			AU 1040392 A	30-07-1992
			CA 2059857 A1	25-07-1992
			DE 59203704 D1	26-10-1995
			DK 496378 T3	05-02-1996
			EP 0496378 A1	29-07-1992
			ES 2079694 T3	16-01-1996
			GR 3017802 T3	31-01-1996
			HU 60462 A2	28-09-1992
			IE 920199 A1	29-07-1992
			JP 4334351 A	20-11-1992
			MX 9200269 A1	01-07-1992
			NO 920320 A , B,	27-07-1992
			NZ 241355 A	26-07-1994
			US 5597825 A	28-01-1997
			US 5736559 A	07-04-1998
			US 5922763 A	13-07-1999
			ZA 9200464 A	23-07-1993
EP 0480258	A	15-04-1992	DE 4032147 A1	16-04-1992
			AU 634424 B2	18-02-1993
			AU 8569291 A	16-04-1992
			BR 9104365 A	09-06-1992
			CA 2052894 A1	11-04-1992
			CS 9103058 A3	14-10-1992
			EP 0480258 A2	15-04-1992
			HU 59671 A2	29-06-1992
			JP 5032631 A	09-02-1993
			MX 9101265 A1	05-06-1992
			ZA 9108069 A	29-07-1992
WO 03068749	A	21-08-2003	WO 03068749 A1	21-08-2003
WO 0208221	A	31-01-2002	AU 8066701 A	05-02-2002
			BR 0112631 A	23-09-2003
			CA 2415606 A1	31-01-2002
			CN 1443170 T	17-09-2003
			EP 1301484 A2	16-04-2003
			WO 0208221 A2	31-01-2002
			US 2002132853 A1	19-09-2002